

REMARKS

Claims 1-27 are pending. Non-elected claims 28-31 have been canceled as a result of the restriction requirement.

Applicants submit that the amendments to step a) of claim 1 would not narrow the scope of the amended recitations because, reading steps a) and b) of claim 1 as originally filed together, a person skilled in the art would have understood that the fermentation broth also contains the assimilable carbon source and assimilable nitrogen source, and that the 6'-O-carbamoyl tobramycin recovered in step c) of claim 1 as original filed is produced with fermentation of the fermentation broth. The amendments to step b) of "regulating a constant level levels of the assimilable carbon source and assimilable nitrogen source in the fermentation broth" would not narrow the scope of the amended recitations because the amendments are either cosmetic (to improve the recitations grammatically) or the inserted phrase of "in the fermentation broth" was inherent in step b) of claim 1 as originally filed. The insertion of "to improve the yield of the 6'-O-carbamoyl tobramycin" in step b) of claim 1 also would not narrow the scope of the amended claim recitation because the insertion is a recitation of the results of regulating the constant levels of the assimilable carbon source and assimilable nitrogen source.

The amendments to claims 4-6, 9, 10, 14, 15 and 20 are cosmetic, made in order to provide proper antecedent bases and would not narrow the scope of the amended claim recitations. The amendments to claims 16-18 and 24-27 are purely grammatical and would not narrow the scope of the amended claim recitations.

The amendments to the claims are supported by the specification at page 6, lines 8-12,

page 8, lines 31-34, page 12, lines 10-11, page 13, lines 13, 14 and 16-18 and Examples 4 and 5.

Claim Rejections - 35 U.S.C. § 103(a)

Applicants respectfully traverse the obviousness rejection of claims 1-27 over Ott *et al.* (GB 2,114,978) taken with Tomita *et al.* (US 4,032,404) and Venek *et al.* ("Selection and Accumulation in Open Systems" in Overproduction of Microbial Metabolites, ed. by Z. Vanek and Z. Hostalek, 1986, pp. 191-195).

Ott *et al.* discloses a process for producing a fermentation broth containing 6'-O-carbamoyl tobramycin by incubating a nutritive medium containing a 6'-O-carbamoyl tobramycin producing strain MNG204 of *Streptomyces tenebrarius*, and organic carbon and nitrogen sources in a submerged, aerated culture at 33 to 40°C, pH 7.2 to 7.4, in a shaker until a substantial amount of 6'-O-carbamoyl tobramycin is accumulated; and then the 6'-O-carbamoyl tobramycin is isolated (page 2, lines 27-38; page 3, lines 4, 5 and 14; page 4, line 15).

Tomita *et al.* discloses a fermentation process for producing 6'-O-carbamoyl tobramycin by culturing a strain of 6'-O-carbamoyl tobramycin producing *Streptoalloteichus hindustanus* in an aqueous nutrient medium containing assimilable sources of carbon and nitrogen in a submerged aerobic culture in sterile tanks (column 10, line 64 to column 11, line 5 and column 11, lines 32-37).

Ott *et al.* and Tomita *et al.* differ from claims 1-27 at least in not teaching or suggesting regulating constant levels of the assimilable carbon source and assimilable nitrogen source in

the fermentation medium. The Office Action attempts to rely on Vanek *et al.* to cure this deficiency but fails as explained below.

The Office Action relies on Vanek *et al.* for the teaching that chemostats were known in the prior art. On the account that chemostats were known, the Office Action concludes that claims 1-27 would have been obvious over Ott *et al.* taken with Tomita *et al.* and Vanek *et al.*. In other words, merely because chemostats were known, the Office Action takes a position that it would have been obvious to regulate constant levels of the assimilable carbon source and assimilable nitrogen source in the fermentation process of Ott *et al.* or Tomita *et al.*.

Applicants respectfully disagree.

The fact that chemostats were known in the prior art only shows that regulating constant levels of the assimilable carbon source and assimilable nitrogen source in the fermentation media of Ott *et al.* and Tomita *et al.* **can be done**. But the mere showing that what is in the prior art is **capable of** being modified to arrive at the claimed invention is not sufficient to support *prima facie* obviousness unless there is a suggestion or motivation for the modification. See *In re Fritch*, 23 USPQ2d 1780 (Fed. Cir. 1992). In the present case, there was no motivation to modify the process of Ott *et al.* or Tomita *et al.* by using a chemostat of Vanek *et al.* to regulate constant levels of the assimilable carbon source and assimilable nitrogen source in the fermentation medium. Neither Ott *et al.* nor Tomita *et al.* suggests regulating constant levels of the assimilable carbon source and assimilable nitrogen source in the fermentation medium, or suggesting any benefit to what they tried to achieve by using a chemostat. Applicants note that Vanek *et al.* teaches using chemostats to select and enrich mutants of the microorganism growing in fermentation media (please see

the title, "Selection and Accumulation in Open Systems" in page 191; page 192, the 2nd to 4th full paragraphs; page 195, the first 3 paragraphs). There is no suggestion in Ott *et al.* or Tomita *et al.* to select and enrich mutants of the microorganisms being cultured in their fermentation media to produce 6'-O-carbamoyl tobramycin. Thus, there was no suggestion or motivation to modify the process of Ott *et al.* or Tomita *et al.* by using a chemostat of Vanek *et al.* to regulate constant levels of the assimilable carbon and nitrogen sources. As a result, claims 1-27 would not have been *prima facie* obvious over Ott *et al.* taken together with Tomita *et al.* and Vanek *et al.*

Another reason why claims 1-27 would not have been *prima facie* obvious over Ott *et al.* taken together with Tomita *et al.* and Vanek *et al.* is that the prior art does not teach that modifying the process of Ott or Tomita by using a chemostat of Vanek to regulate constant levels of the assimilable carbon and nitrogen sources would result in an improved yield of the 6'-O-carbamoyl tobramycin as claimed (see step b) of claim 1). Ott *et al.*, Tomita *et al.* and Vanek *et al.* are silent on improving the yield of the 6'-O-carbamoyl tobramycin in the process of Ott *et al.* or Tomita *et al.*

Since the Office Action fails to show that claims 1-27 would have been *prima facie* obvious over the prior art references relied upon, claims 1-27 should not have been rejected as obvious.

A further reason why claims 1-27 would not have been obvious over Ott taken together with Tomita and Vanek is that the improved yields of the 6'-O-carbamoyl tobramycin achieved by regulating constant levels of the assimilable carbon and nitrogen sources (please see Examples 4 and 5 in comparison with Examples 1-3) discovered by the

present inventors were unexpected results. The prior art does not teach or suggest that regulating constant levels of the assimilable carbon and nitrogen sources in a fermentation medium containing a 6'-O-carbamoyl tobramycin producing microorganism would result in improved yields of the 6'-O-carbamoyl tobramycin. Withdrawal of the obviousness rejection is requested.

Conclusion

In light of the above reasoning, applicants submits that the application is in a condition for allowance. A Notice of Allowance is believed in order. If the Examiner deems that there are issues that can be resolved by a telephone interview, the Examiner is urged to telephone the undersigned at.

In the event that this paper is deemed not timely, applicants petition for an appropriate extension of time. The petition fee and any other fees that may be required in relation to this paper can be charged to Deposit Account No. 11-0600, referencing the Attorney Docket No. 02664/47002.

Respectfully Submitted,

Dated: November 30, 2004

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